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(54) Title: PROTOZOAN RHOMBOID PROTEINS

(57) Abstract: Protozoan Rhomboid Proteins This invention relates to the identification of protozoan Rhomboid proteins that are involved in the invasive processes of protozoan pathogens, such as *P. falciparum*. Modulation of these Rhomboid proteins may thus be useful in treating protozoan pathogen infection. Methods and means relating to the modulation of protozoan Rhomboid proteins is provided herein.

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# INTERNATIONAL SEARCH REPORT

International Application No  
PC 03/04711

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C12Q1/37 C12N9/50

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, EPO-Internal, BIOSIS, MEDLINE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FR 2 791 685 A (PASTEUR INSTITUT) 6 October 2000 (2000-10-06) the whole document	1-4, 17-19
A	BLACKMAN M J ET AL: "Secondary processing of the Plasmodium falciparum merozoite surface protein-1(MSP1) by a calcium-dependent membrane-bound serine protease: shedding of MSP133 as a noncovalently associated complex with other fragments of the MSP1" MOLECULAR AND BIOCHEMICAL PARASITOLOGY, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 50, no. 2, 1992, pages 307-315, XP000603761 ISSN: 0166-6851 the whole document	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the International filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

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- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- \*G\* document member of the same patent family

Date of the actual completion of the international search

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/JP 03/04711

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>BLACKMAN M J ET AL: "A conserved parasite serine protease processes the Plasmodium falciparum merozoite surface protein-I" MOLECULAR AND BIOCHEMICAL PARASITOLOGY, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 62, no. 1, November 1993 (1993-11), pages 103-114, XP000856228 ISSN: 0166-6851 the whole document</p>	
A	<p>OPITZ CORINNA ET AL: "Intramembrane cleavage of microneme proteins at the surface of the apicomplexan parasite Toxoplasma gondii" EMBO (EUROPEAN MOLECULAR BIOLOGY ORGANIZATION) JOURNAL, vol. 21, no. 7, 2 April 2002 (2002-04-02), pages 1577-1585, XP002276565 ISSN: 0261-4189 the whole document</p>	
A	<p>CARRUTHERS VERN B ET AL: "The Toxoplasma adhesive protein MIC2 is proteolytically processed at multiple sites by two parasite-derived proteases" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 275, no. 19, 12 May 2000 (2000-05-12), pages 14346-14353, XP002276566 ISSN: 0021-9258 the whole document</p>	
A	<p>URBAN SINISA ET AL: "Conservation of intramembrane proteolytic activity and substrate specificity in prokaryotic and eukaryotic Rhomboids" CURRENT BIOLOGY, vol. 12, no. 17, 3 September 2002 (2002-09-03), pages 1507-1512, XP002245174 ISSN: 0960-9822 the whole document</p>	
A	<p>URBAN S ET AL: "Intramembrane proteolysis controls diverse signalling pathways throughout evolution" CURRENT OPINION IN GENETICS &amp; DEVELOPMENT, CURRENT BIOLOGY LTD, XX, vol. 12, no. 5, 1 October 2002 (2002-10-01), pages 512-518, XP002245175 ISSN: 0959-437X the whole document</p>	

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# INTERNATIONAL SEARCH REPORT

International Application No.  
PCT/GB 03/04711

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>KOONIN EUGENE V ET AL: "The rhomboids: a nearly ubiquitous family of intramembrane serine proteases that probably evolved by multiple ancient horizontal gene transfers."</p> <p>GENOME BIOLOGY ENGLAND 2003, vol. 4, no. 3, 28 February 2003 (2003-02-28), page R19 XP002276564 ISSN: 1465-6914 the whole document</p>	32,34
P,X	<p style="text-align: center;">---</p> <p>URBAN SINISA ET AL: "Substrate specificity of Rhomboid intramembrane proteases is governed by helix-breaking residues in the substrate transmembrane domain."</p> <p>MOLECULAR CELL, vol. 11, no. 6, June 2003 (2003-06), pages 1425-1434, XP009022588 ISSN: 1097-2765 (ISSN print) the whole document</p>	1-4, 6-19,32, 34-36
P,A	<p style="text-align: center;">---</p> <p>WO 02/093177 A (MEDICAL RES COUNCIL ;FREEMAN MATTHEW (GB)) 21 November 2002 (2002-11-21) the whole document</p> <p style="text-align: center;">-----</p>	

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB 03/04711

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 5, 20-31, 33  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 5, 20-31, 33

Claims 5 and 33 refer to nucleic acid sequences shown in table 1. Table 1a does not appear to identify any sequence of a Rhomboid polypeptide. Consequently, a meaningful search over the whole scope of claims 5 and 33 is not possible.

Claims 20-31 relate to a product defined by reference to a desirable characteristic or property, namely inhibiting cleavage of the substrate by Rhomboid polypeptide, and methods of modifying/using said product. The claims cover all products having this characteristic or property, whereas the application provides no support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for any such products. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the product by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search impossible.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

## INTERNATIONAL SEARCH REPORT

Inter Application No  
PCT/03/04711

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
FR 2791685	A	06-10-2000	FR 2791685 A1	06-10-2000
WO 02093177	A	21-11-2002	CA 2447040 A1	21-11-2002
			WO 02093177 A2	21-11-2002